

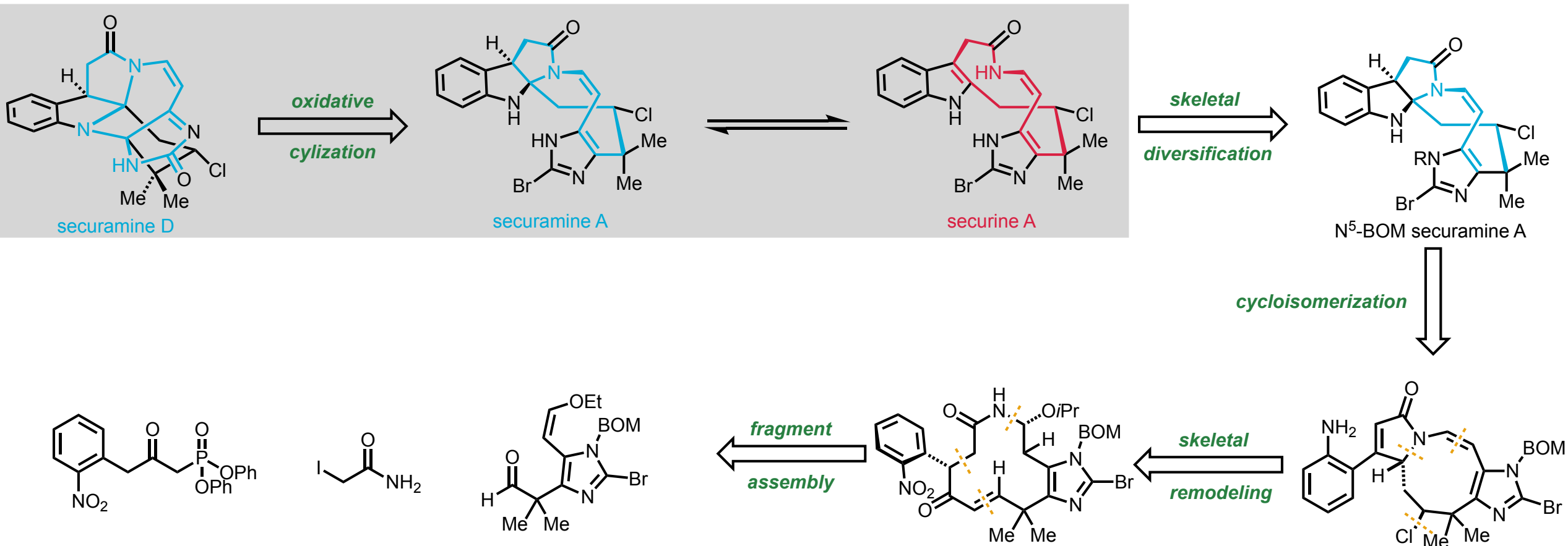
Discovery: extracts from bryozoan *Securiflustra securifrons*, Cytotoxic agents.

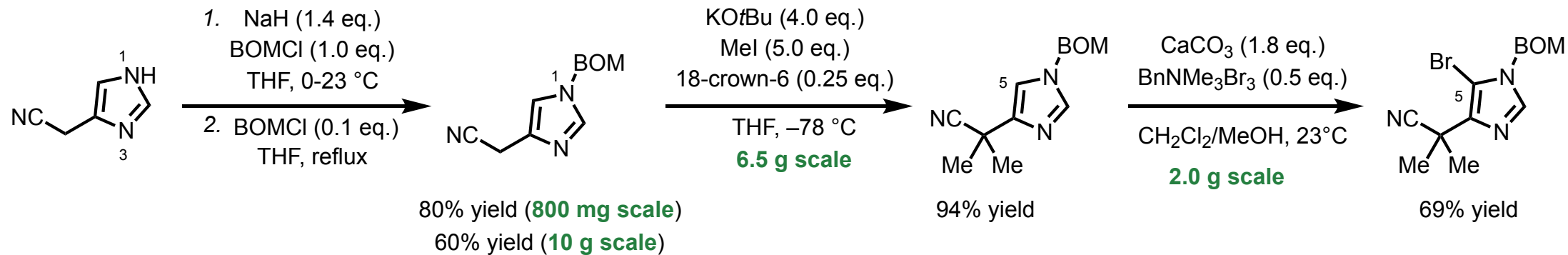
Significance: indoline halogenation and electrophilic character at C2 cooperatively enhance activity, but the mechanism of action and intracellular target of the molecules is not known.

Synthetical challenge: an unstable cis-enamide, a neopentyl secondary alkyl chloride, a basic haloimidazole and a labile halogenated indoline residue.

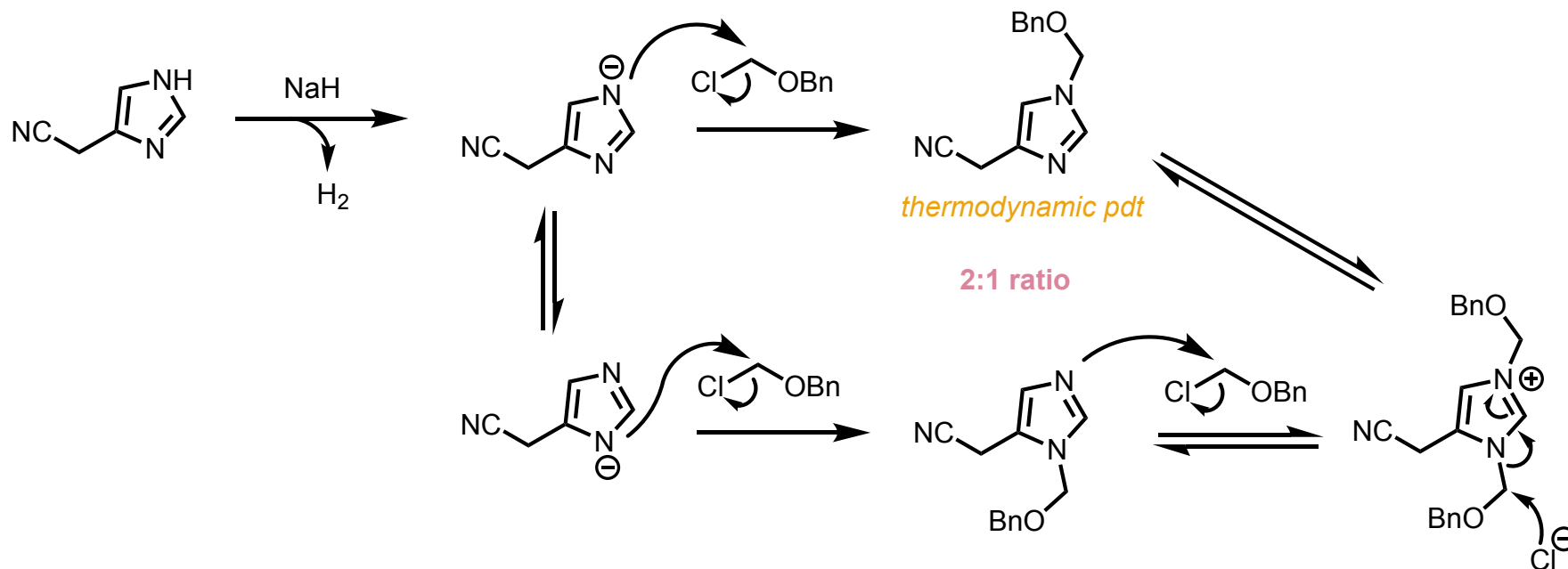
Highlight in the route: cascade sequence to construct the key skeleton.

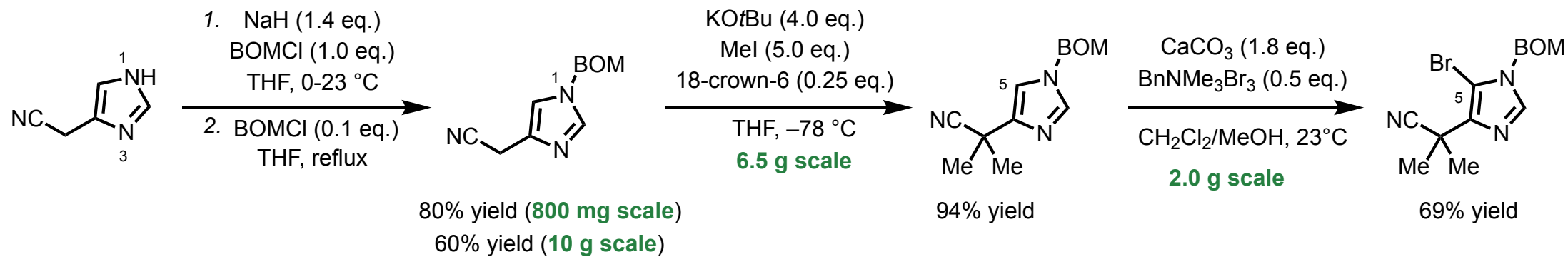
Retrosynthetic Analysis:



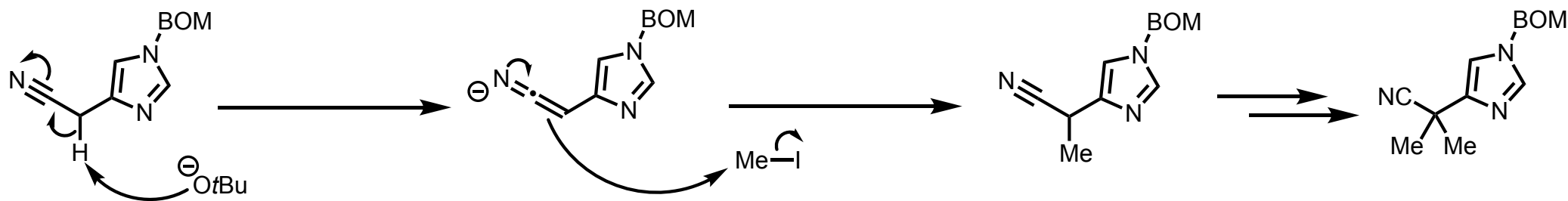


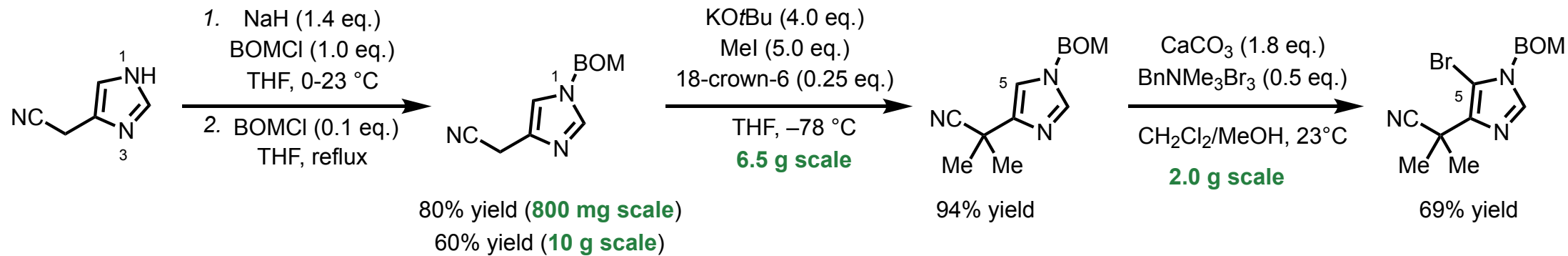
BOM Protection:



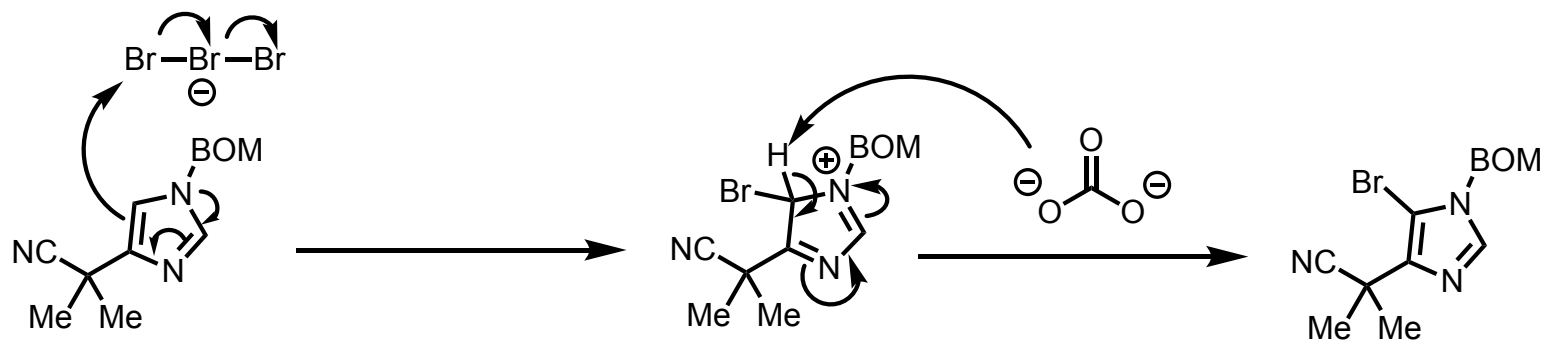


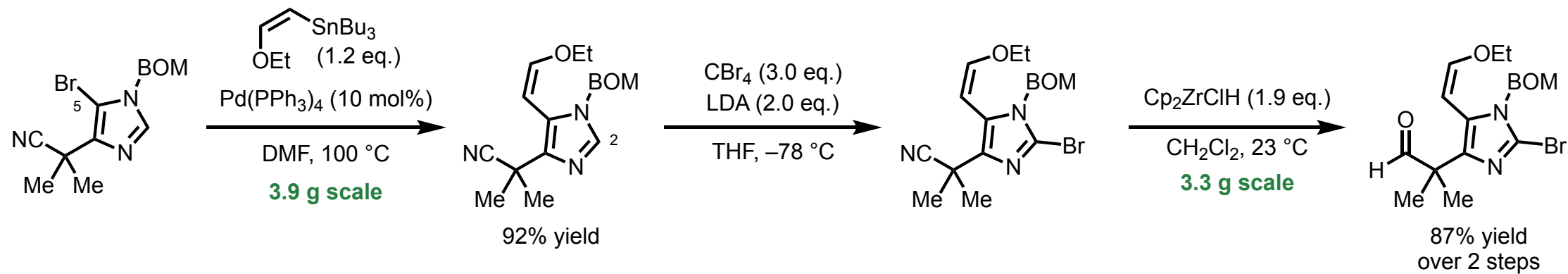
Methylation:



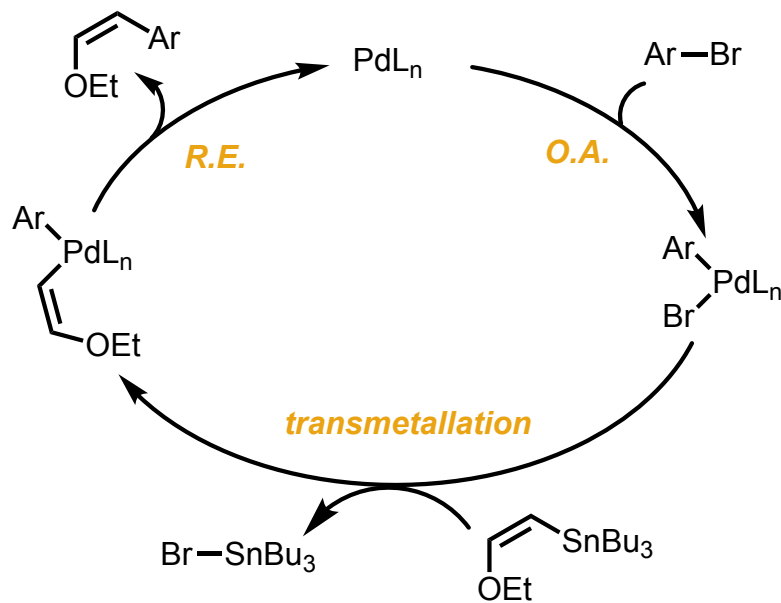


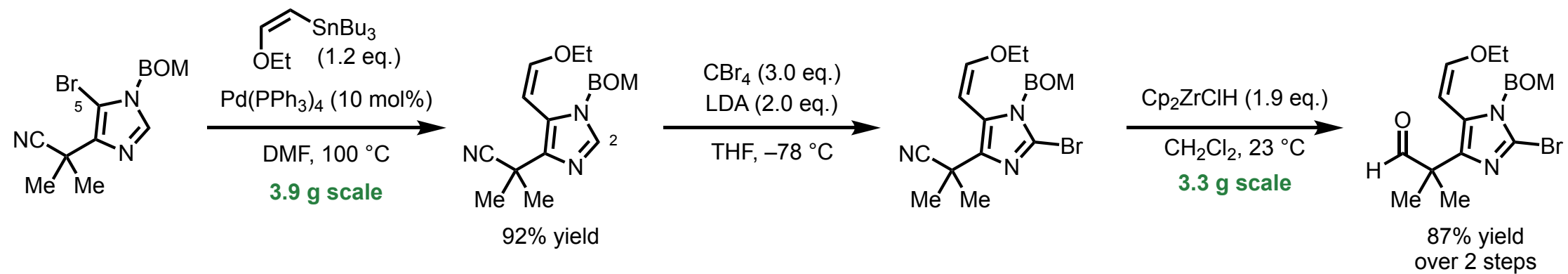
Bromination:



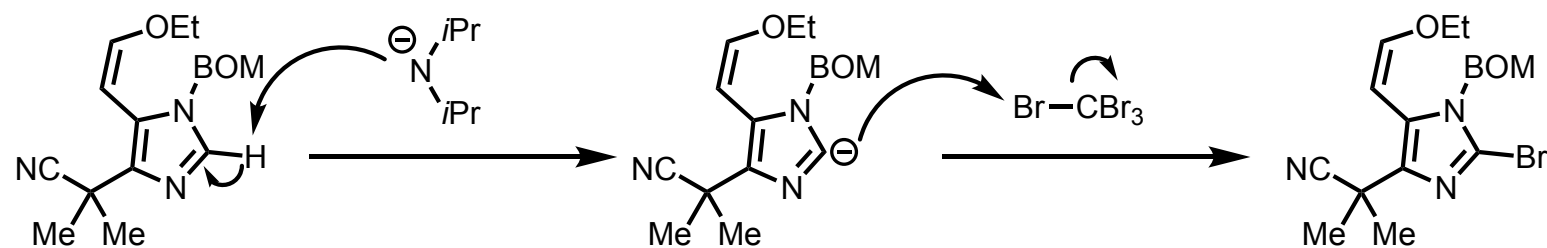


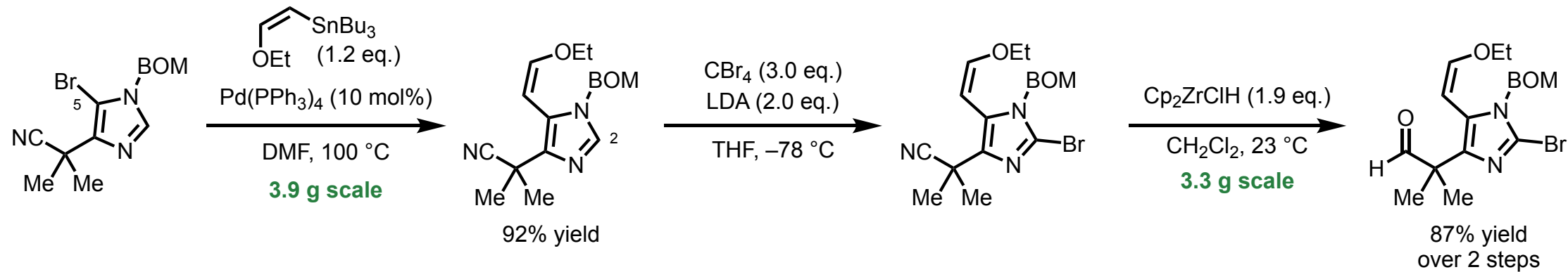
Stille Coupling:



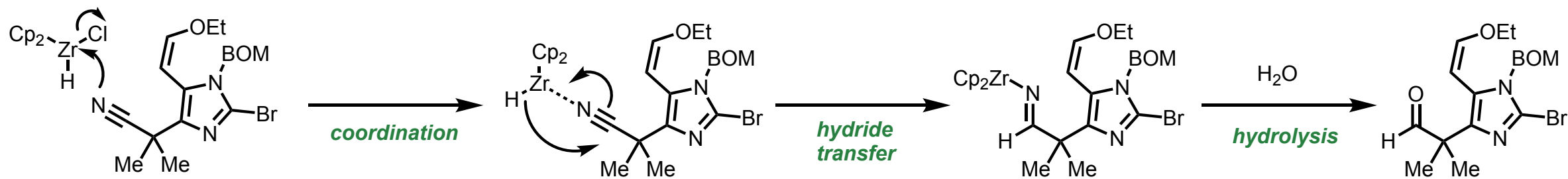


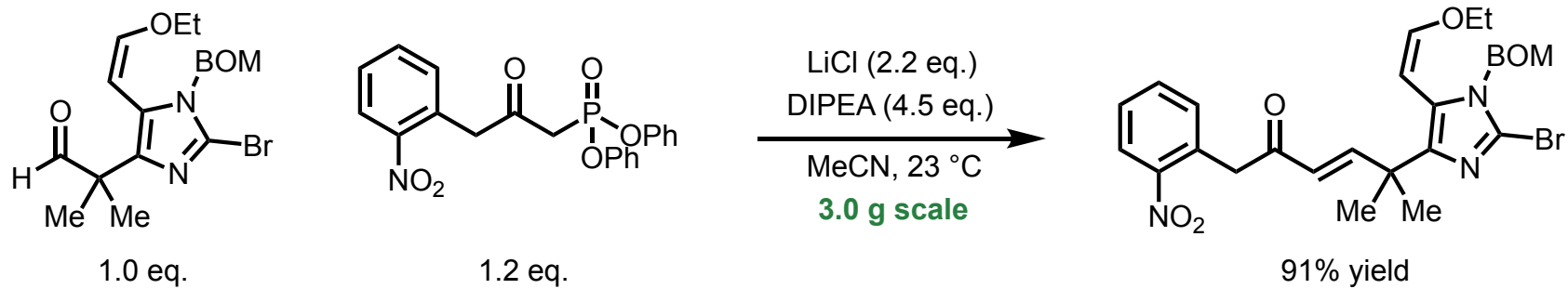
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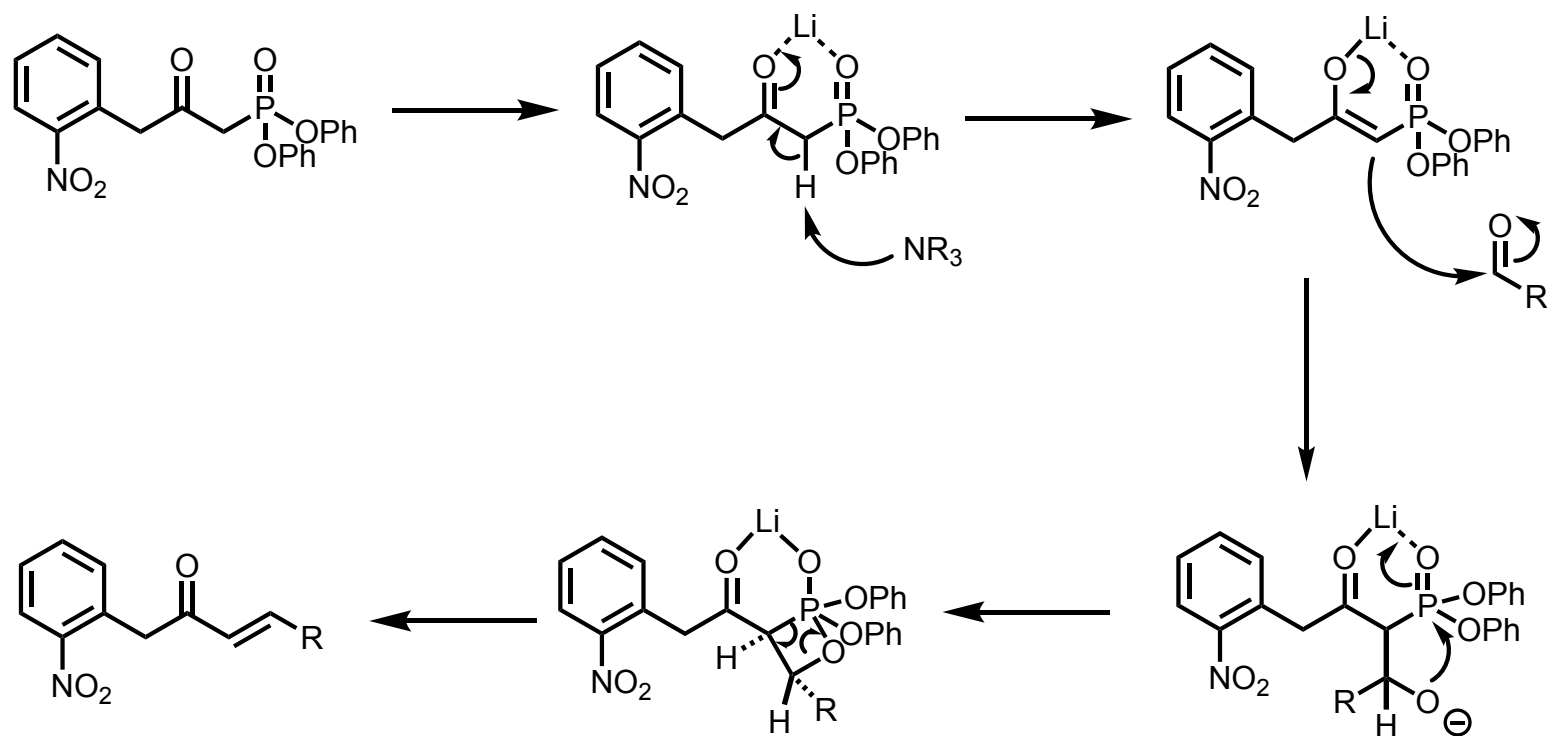


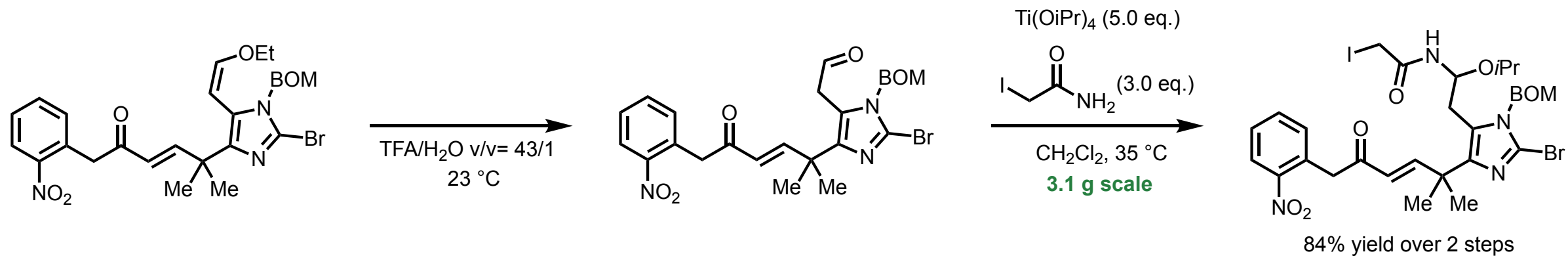
Nitrile Reduction:



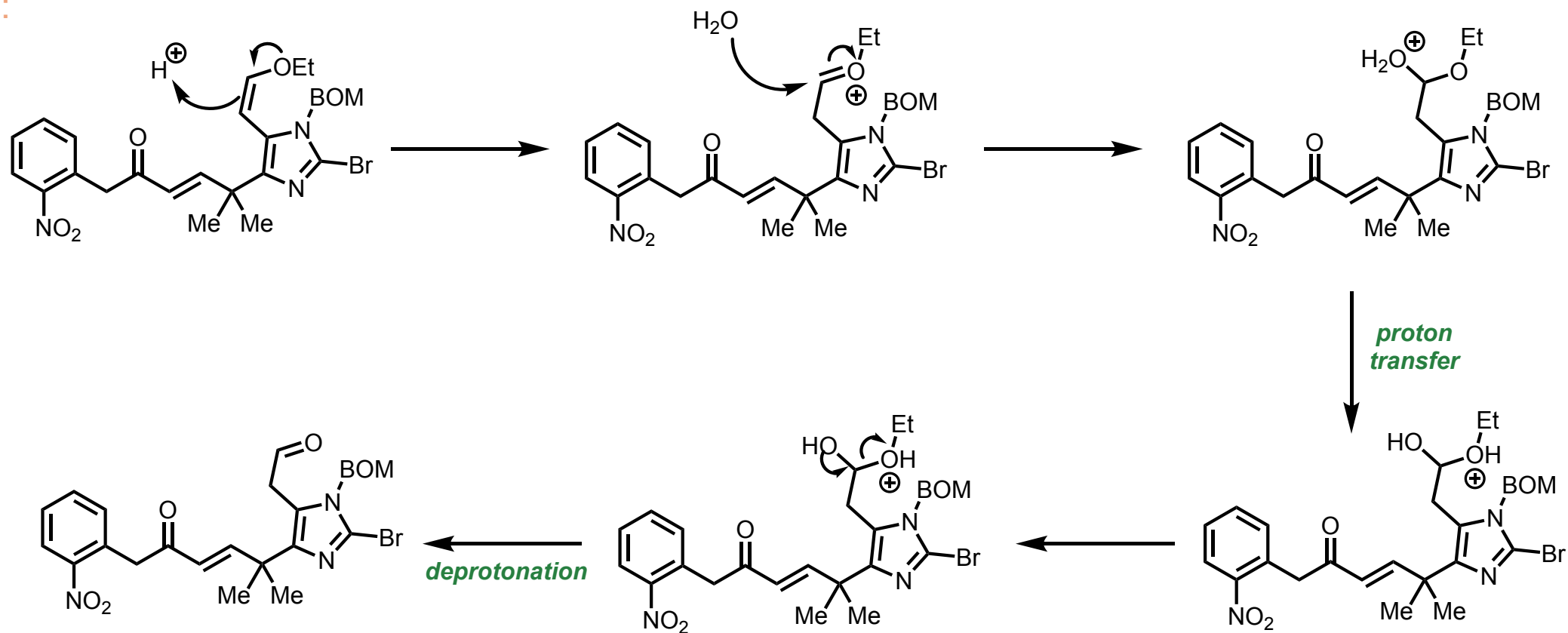


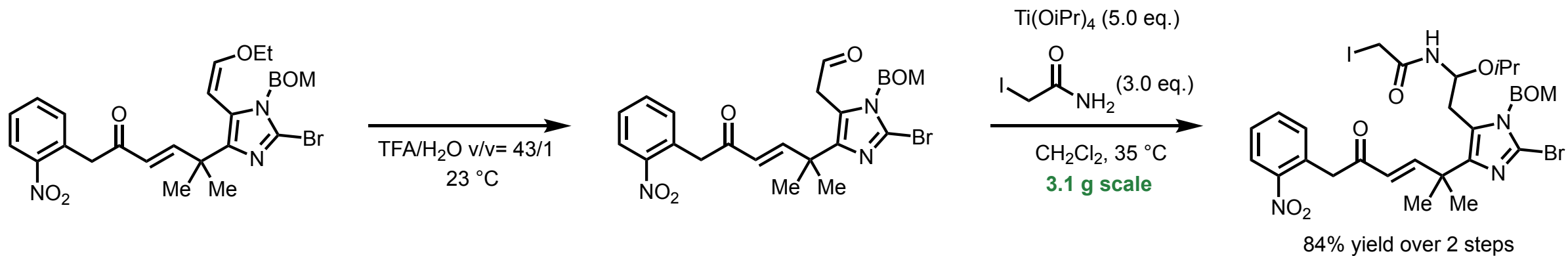
Horner-Wadsworth-Emmons Reaction (Masamune-Roush Modification):



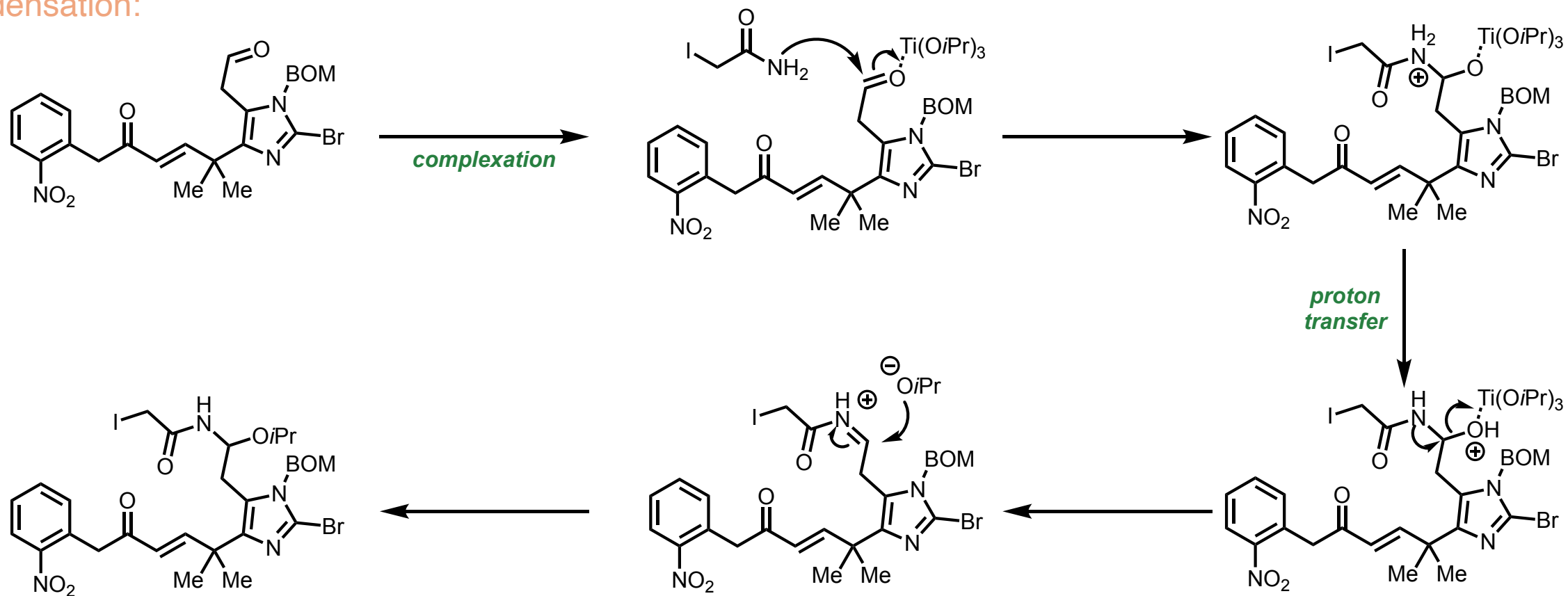


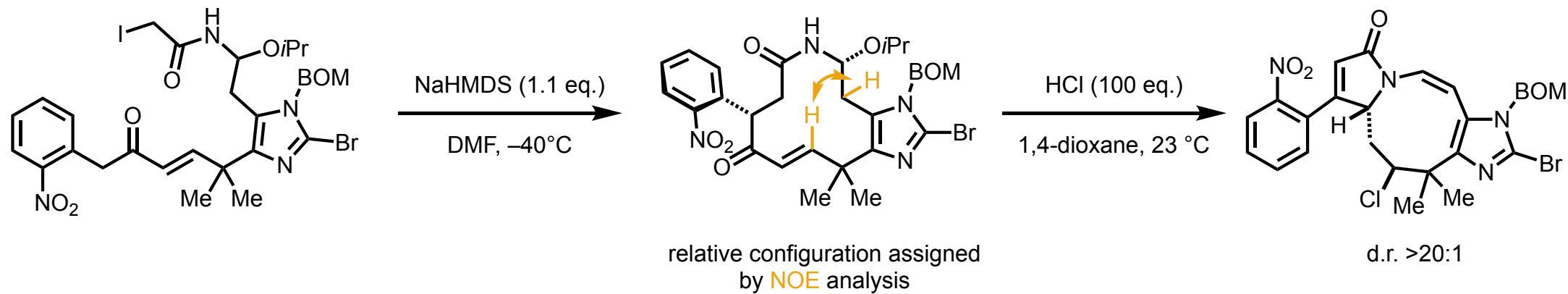
Hydrolysis:



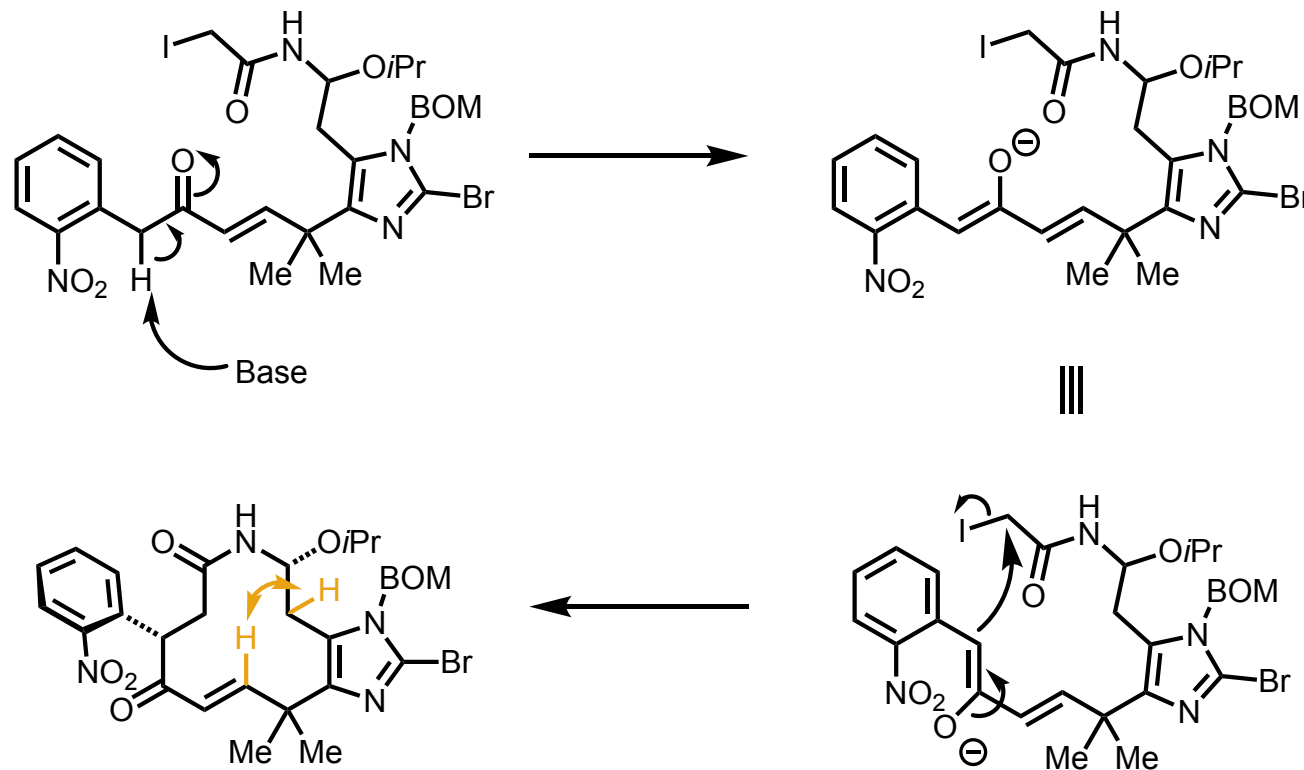


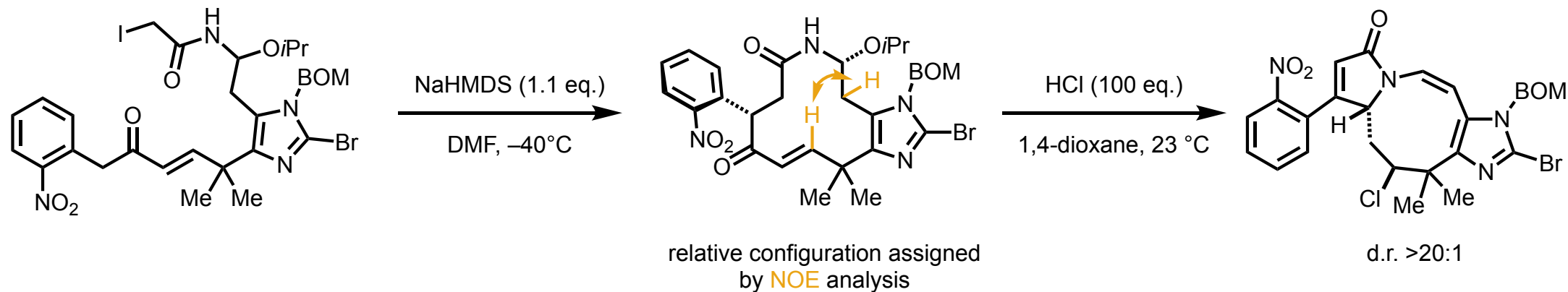
Condensation:



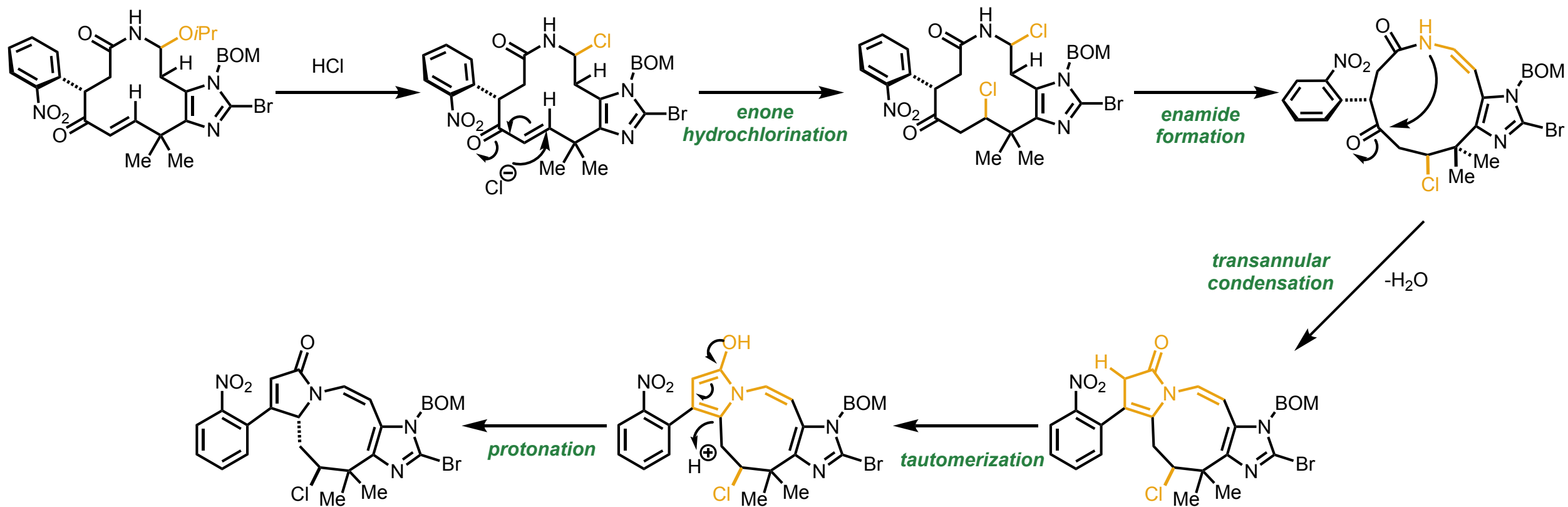


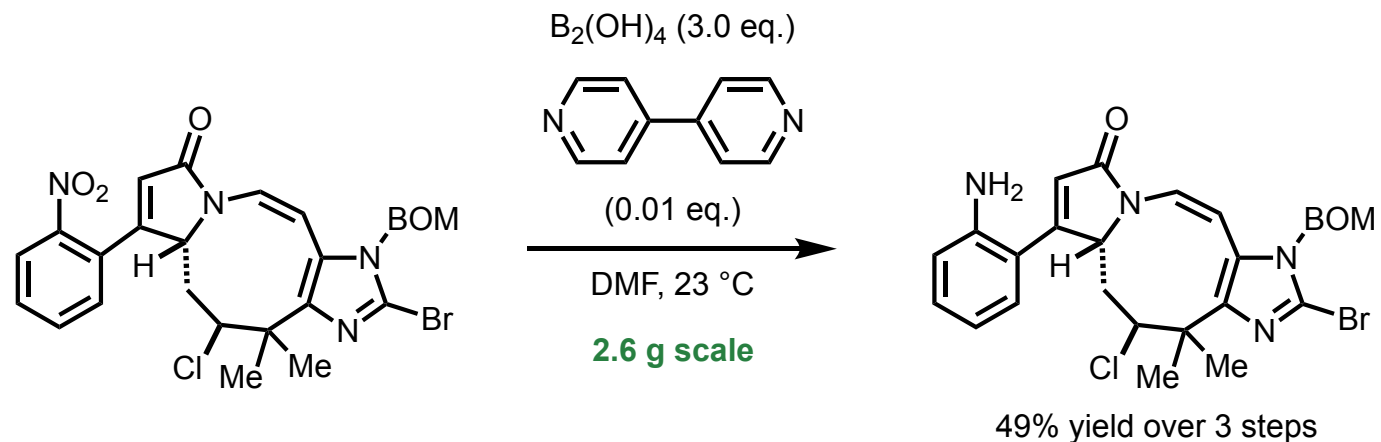
Alkylation:





Elimination-Michael Addition-Isomerization Cascade:



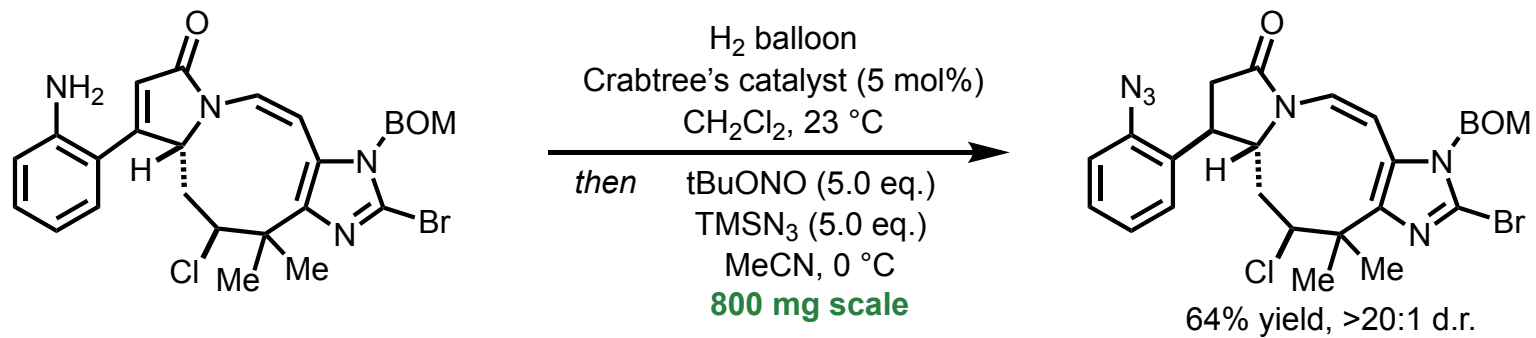


Nitro Group Reduction:

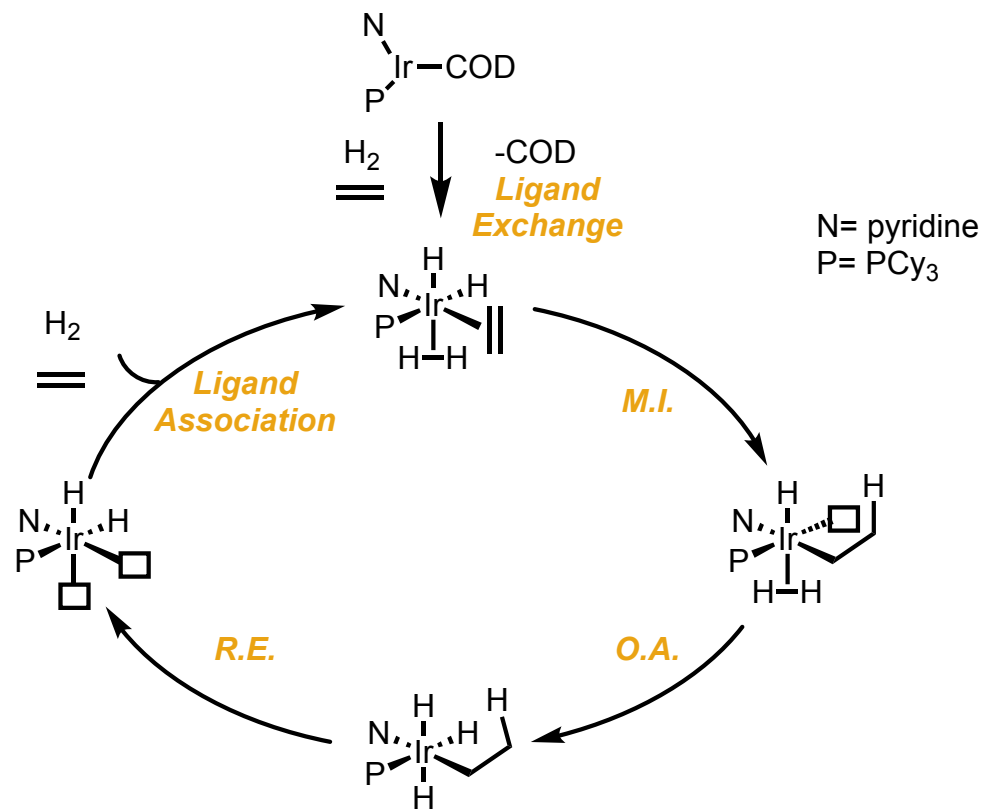
Mechanism unknown:

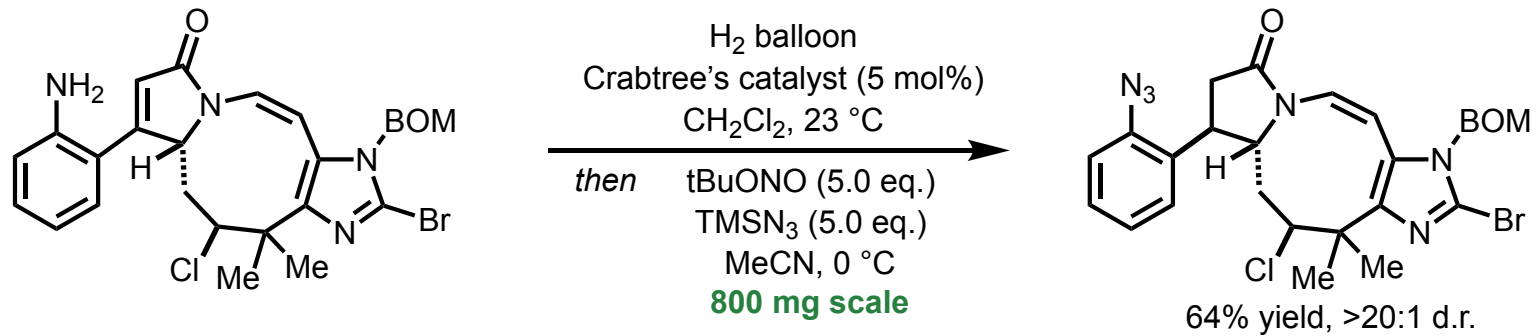
1. NH₂ proton source is B₂(OH)₄ (suggested by deuterium labelling)
2. Possibly involves a radical mechanism. (indicated by TEMPO inhibition)

J. Org. Chem. **2022**, 87,910–919.

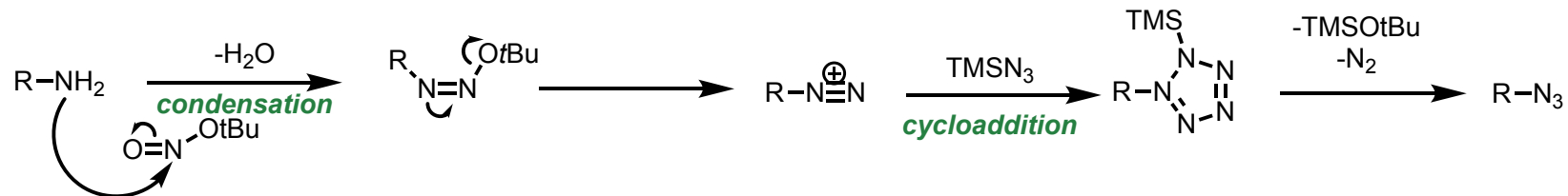


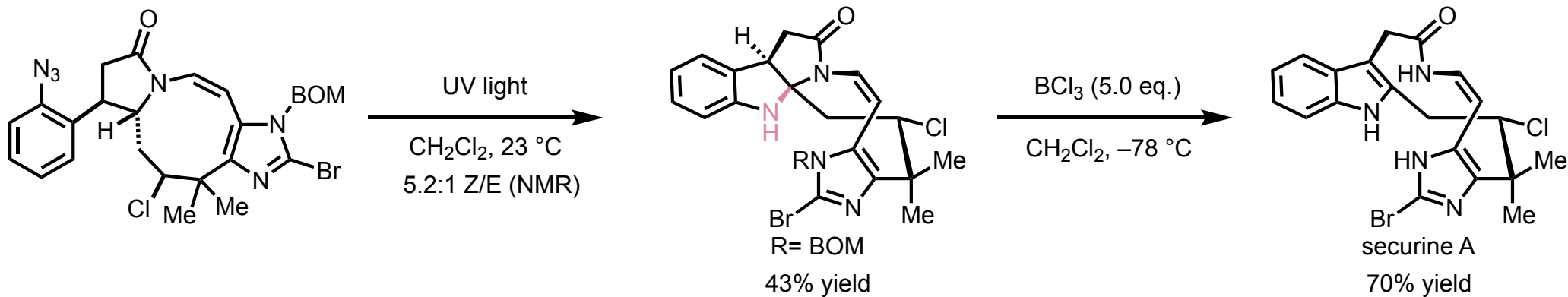
Hydrogenation:



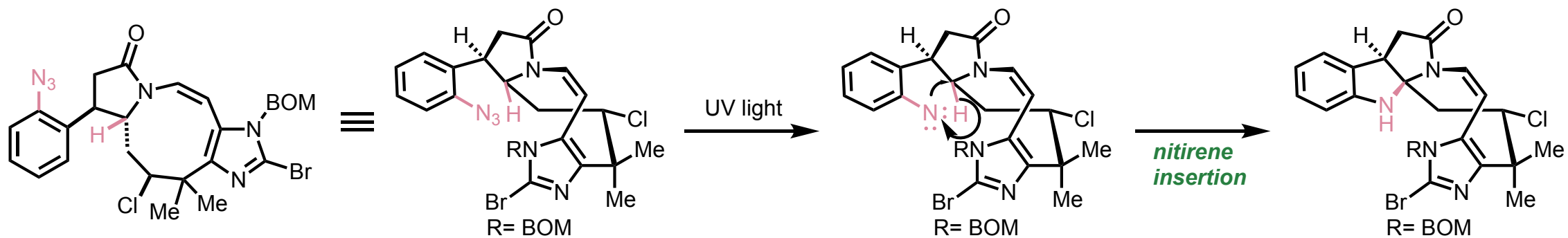


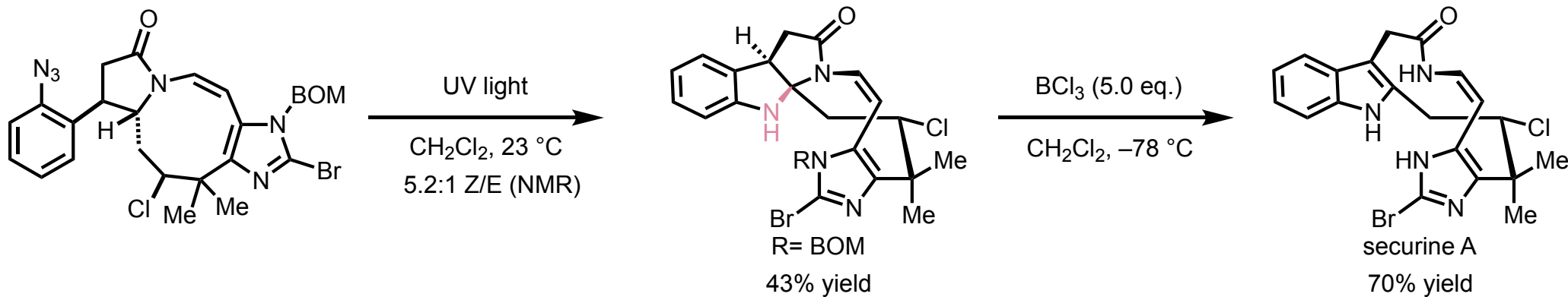
Sandmeyer Reaction:



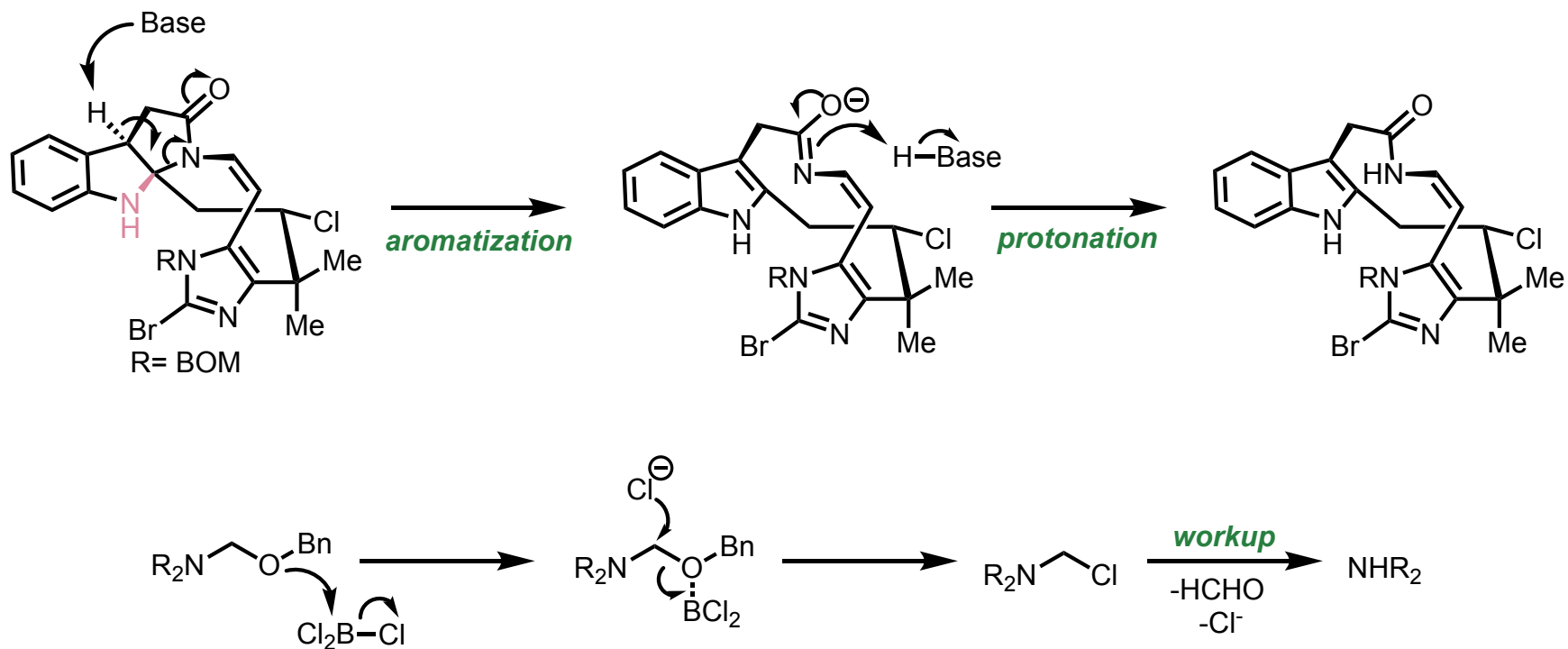


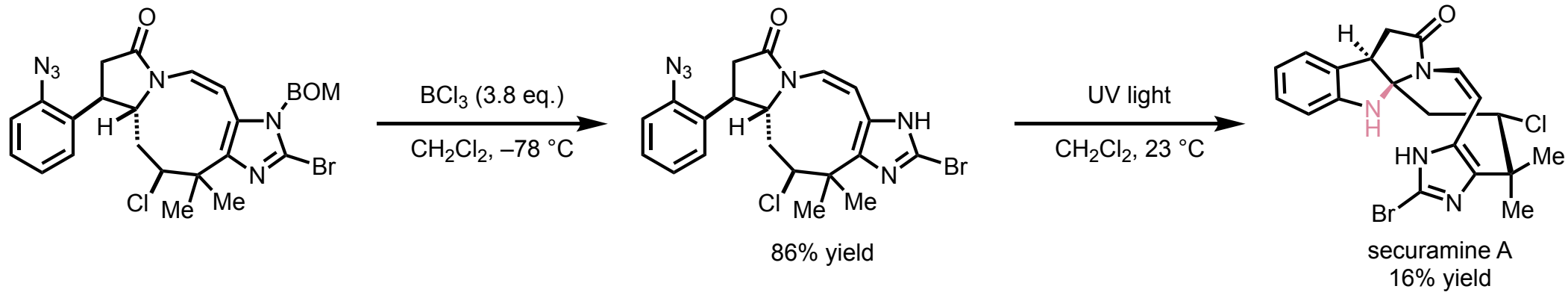
Nitrene Insertion:



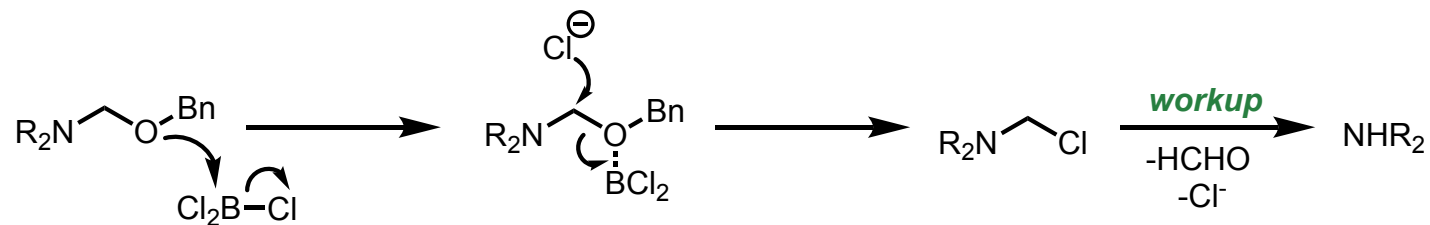


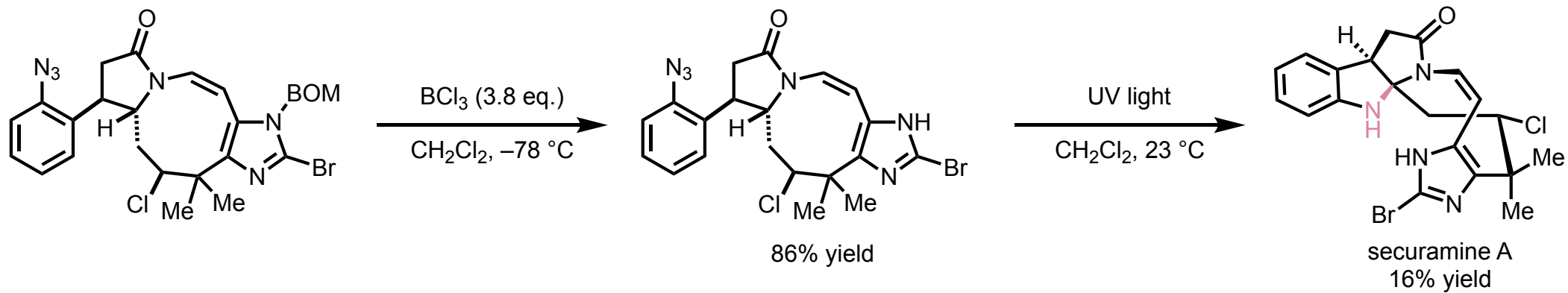
BOM Deprotection/Aromatization:



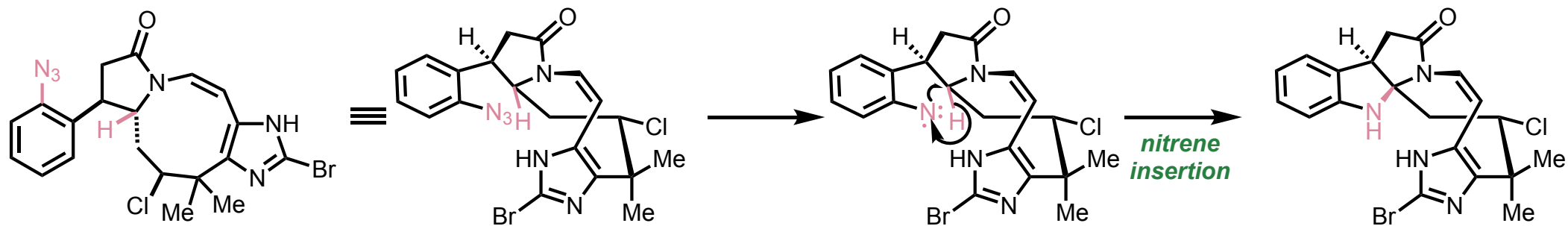


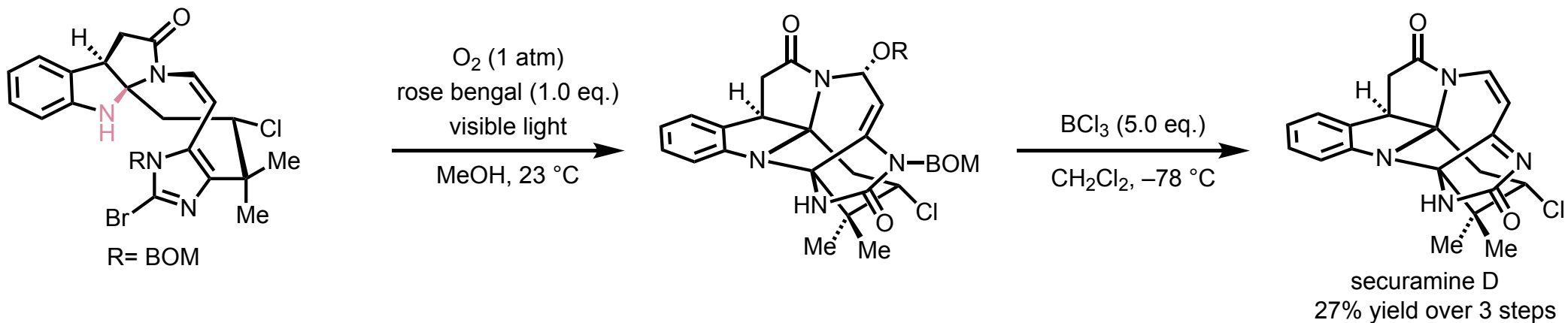
BOM Deprotection:



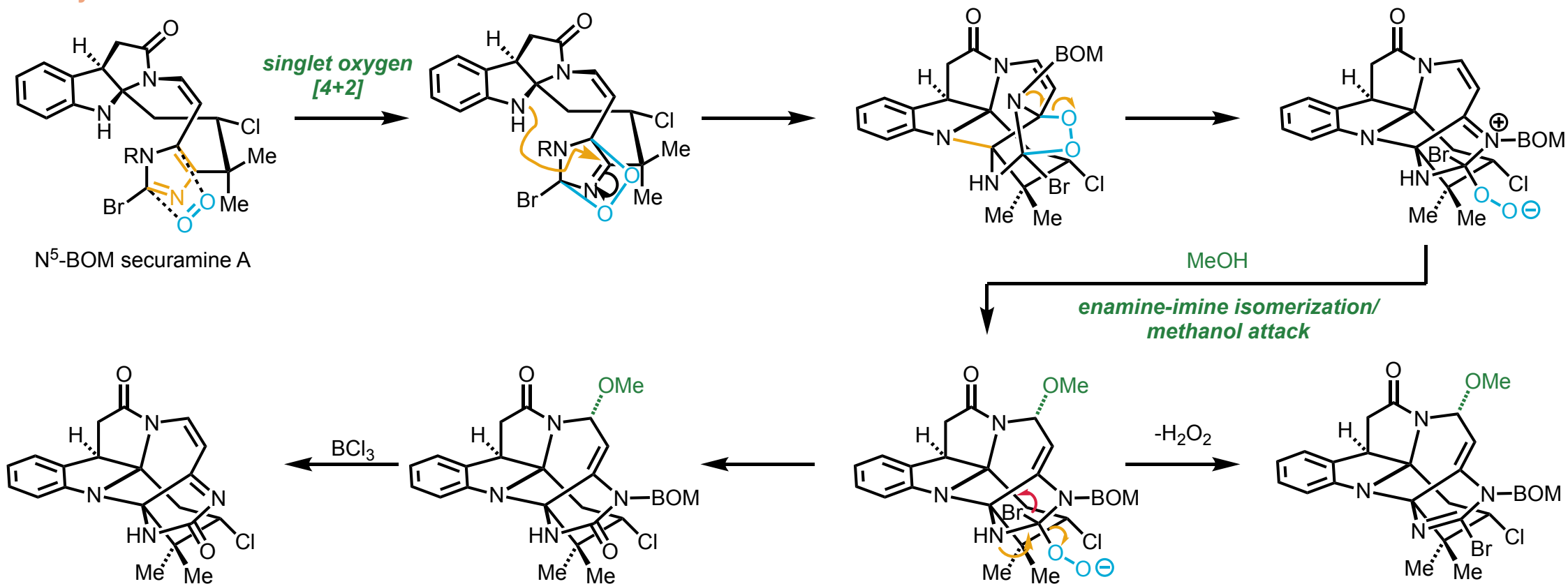


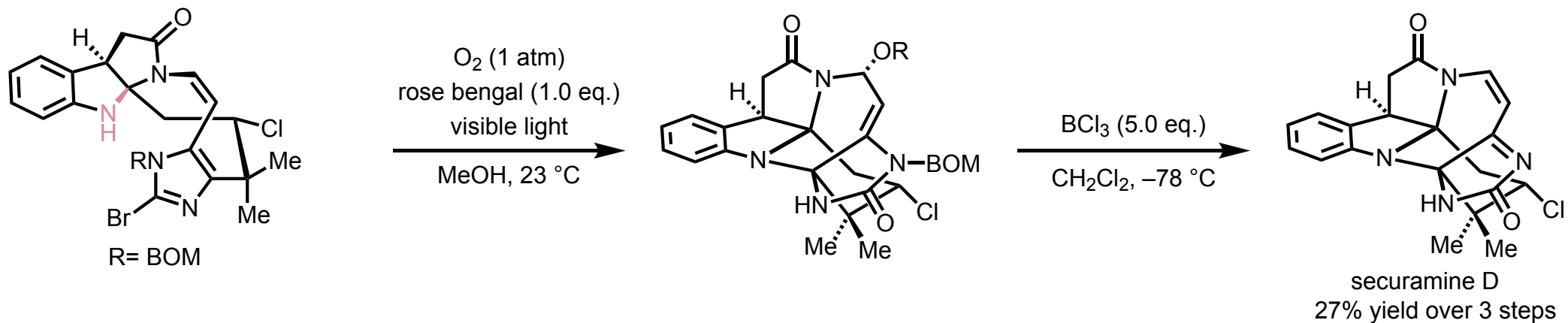
Nitrene Insertion:





Oxidative Cyclization:





BOM Deprotection:

